A Theory of Protein Metabolism in Man

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where l_1 and l_2 are the respective lengths of the layers $k_1 = 2\pi/\lambda_1$ and $k_2 = 2\pi/\lambda_2$, and $Z_1 = \rho_1 c_1/S_1$, $Z_2 = \rho_2 c_2/S_2$. The quantity Z is recognized as the so-called acoustic impedance of a plane compressional wave. Here again the formal agreement is evident and the analogy becomes more striking if $S_2/S_1 = \rho_2/\rho_1$. The structure here considered is of course a low-pass compressional wave filter. If cos U is plotted against frequency (instead of energy as in the electron case) cos U is numerically not greater than unity for frequencies extending from zero to some "cut-off" frequency where there begins a "forbidden" band, i.e., a range of frequencies for which no transmission takes place. The plot of (5) on a frequency scale is formally equivalent to that of (4) on an energy scale. Irreversible dissipation is, of course, ruled out in both problems.

The above analogy breaks down in the case where $W > V_1$ but $W < V_2$. In this case transmission through the lattice is controlled by

$$\cos U = \cos \alpha_1 l_1 \cosh \alpha_2 l_2 - \frac{1}{2}\left(\frac{\alpha_1}{\alpha_2} - \frac{\alpha_2}{\alpha_1}\right) \sin \alpha_1 l_1 \sinh \alpha_2 l_2 \quad (4')$$

since α_2 is now imaginary. In order to provide an elastic wave analogy it is necessary to contemplate an elastic medium in which the compressional wave velocity is infinite (i.e., there is no variation in phase from one point to another) but in which the displacement amplitude is attenuated with distance.

[1] See, for example, Frenkel, *Wave Mechanics: Elementary Theory*, Oxford, 1932, p. 99 ff.

[2] See, for example, Stewart and Lindsay, *Acoustics*, N. Y., 1930, p. 77.

[3] See Lindsay, Lewis and Albright, *Jour. Acous. Soc. Amer.*, January (1934).

A THEORY OF PROTEIN METABOLISM IN MAN

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Experiments which will be published in detail elsewhere have led to the following conception of protein metabolism in man.

During a 24-hour period when the subject is maintained in nitrogen balance with either protein, or a mixture of amino acids, or a single amino acid, the larger fraction (60–75%) of the nitrogen metabolized in this period is derived not from the nitrogen ingested during this interval, but from that already present. In this sense the bulk of the protein metabo-

lized in any one day is endogenous. The term endogenous is used here in a different sense from the connotation given it by Folin, who used it to designate the wear and tear quota of protein metabolized. The simplest direct evidence for the above conclusion was furnished by experiments in which a mixture of amino acids and protein was ingested containing only a small amount of sulphur. These experiments showed that under these conditions there is no sparing of the basal sulphur. In several instances more sulphur was excreted than the sum of the amount ingested and the total excreted during a fasting period of 24 hours. It follows therefore that when protein is ingested the nitrogen and sulphur excreted do not come for the most part from the ingested protein; but that approximately three quarters is derived from protein (or protein split products) already in the organism.

The sulphur figures suggest that the ingestion of protein or amino acids is followed by a stimulation of endogenous protein metabolism. Experiments carried out to estimate the extent of this stimulation showed that it does not exceed ten per cent of the total protein metabolized, and in most cases is probably much less.

The sulphur data support the theory of the existence of depôts of "storage" protein in the organism; the amount of this storage is a function of the level of the nitrogen equilibrium. These depôts, even when the subject is in nitrogen equilibrium, are being constantly replenished and depleted. In starvation they furnish, of course, all the protein metabolized; but even when a large quantity of protein is ingested, most of the protein catabolized in a day is derived from storage protein.

The increase in uric acid following the ingestion of amino acids or proteins, which has been interpreted as evidence of a stimulation of endogenous

TABLE 1

URINARY URIC ACID

FASTING AND AFTER THE INGESTION OF AMMONIUM CARBONATE

TIME	FASTING MG.	AFTER AMMONIUM CARBONATE MG.
9 A. M.–11 A. M.	34	37
11 A. M.– 1 P. M.	41	40
1 P. M.– 3 P. M.	32	51
3 P. M.– 5 P. M.	20	45
5 P. M.– 7 P. M.	21	42
7 P. M.–11 P. M.	37	63
11 P. M.– 8 P. M.	52	54

protein metabolism,[1] is for the most part the consequence only of an increased liberation of ammonia as a result of deamination. Administration of ammonia alone is followed by an increase in urinary uric acid.

Table 1 is an abstract of the results of one of a large number of experiments in which 10–11 gm. of nitrogen in the form of ammonium carbonate was ingested. The ammonium carbonate was made up in an agar gel which was ingested over a period from 9 A. M. to 4 P. M.

Taken in conjunction with the experiments reported previously[2,3,4] the present experiments account for the salient aspects of the specific dynamic action of protein. Table 2 is a partial protocol of an experiment in which

TABLE 2

ENERGY METABOLISM, AND URINARY NITROGEN, SULPHUR AND URIC ACID FOLLOWING THE INGESTION OF 87 GM. GELATINE BETWEEN 8 A. M. AND 9 A. M.

TIME	CALORIES KG. CAL.	URINARY NITROGEN GM.	TOTAL URINARY SULPHUR MG.	TOTAL URINARY URIC ACID MG.
6.30 A. M.	62.9			
6.00–7.10				17.1
8.00				13.5
8.30	77.2			
9.00		0.60	29.6	35.8
9.30	80.4			
10.00		.83	31.8	42.7
10.30	80.5			
11.00		.98	36.9	40.9
11.30	75.5			
12.00		1.14	41.6	36.5
12.30	73.4			
1.00		0.87	38.2	20.9
1.30	70.0			
2.00		.78	45.6	20.8
2.30	70.7			
3.00		.76	51.1	23.1
3.30	69.8			
4.00		.73	49.0	21.1
4.30	70.0			
5.00		.65	49.9	13.3
5.30	70.1			
6.00				19.2

87 gm. of gelatine were ingested between 8 and 9 A. M. The results are typical of many, and it gives one of the main points bearing on the problem of the specific dynamic action of protein. The increase in uric acid closely parallels the caloric increase in metabolism. The nitrogen and sulphur excretion lag behind. We have found also that the ratio of calories in excess of the basal to nitrogen excreted in excess of the basal is not constant. It is less on a high than on a low nitrogen balance. These and other data lead us to propose the following theory regarding the specific dynamic action of protein. The increase in metabolism observed is a

composite of two groups of factors, one of which is a constant and the other variable. The constant factor comprises the increased oxygen consumption attending the oxidative deamination of the amino acids, and the conversion of the ammonia to urea. In these two processes one molecule of additional oxygen is used for every additional molecule of nitrogen deaminized and converted to urea, or approximately 7 calories per gram of nitrogen. Of the variable fraction, one part is the increase in the metabolism of the kidney while excreting the increased quantity of nitrogen. The experiments of Dock[5] have shown that the ratio of the increase in metabolism to the increase in thermodynamic work performed by the kidney diminishes as the amount of work performed increases. Under the conditions of our experiments the increased kidney work would probably not account for more than 5 calories per gram of nitrogen. The other part of the variable fraction is the stimulation of metabolism by the sudden increase in the cells, particularly of the kidney and liver, of the amount of keto acids resulting from deamination.

Under conditions where the "chemical" heat regulation mechanism of Rubner is in operation, i.e., at temperatures below 20°C., where fat and carbohydrate exert no specific dynamic action, we would predict that the specific dynamic action of protein will consist only of the constant fraction described above plus a small additional factor for the work of the kidney, i.e., between 7 and 12 kg. calories per gram of additional nitrogen metabolized. This is in excellent agreement with the values found by Rubner[6] on the dog and Terroine and Bonnet[7] on the frog. At temperatures above 25°C. where the "chemical" heat regulating mechanism is inoperative and the body temperature is governed only by the "physical" heat regulating mechanisms we should expect higher values for the specific dynamic action of protein; because here fat and carbohydrate and therefore deaminized residues now exert some stimulating influence on the metabolism. This prediction also is in full accord with the experimental findings. In dogs at 25° or higher the specific dynamic action of alanine and glycine is 14–32 kg. calories per gram of nitrogen metabolized.[8] In men after feeding gelatine we have obtained values between 18 and 32 kg. calories of excess metabolism per gram of excess nitrogen metabolized. The observation mentioned above that the specific dynamic action per gram of nitrogen metabolized is less on a high than on a low nitrogen balance can be explained reasonably on the view that a given quantity of keto acid will exert a lower stimulating effect when the fasting metabolism of deaminized residues is high than when it is low. This concept similarly affords an explanation for the observation of Wilhelmj and Mann[9] that the specific dynamic action of alanine and glycine is greater in a starving than in a well fed animal. Nevertheless, even the lowest values at the higher temperatures are higher than those obtained below 20°C., which is in accord with the theory.

Summary.—A theory of protein metabolism in man is proposed, some of whose features are:

(1) Most of the protein metabolized in any one day, even when the subject is in nitrogen equilibrium and a sufficient quantity of protein is ingested to maintain this equilibrium, is of endogenous origin, in the sense that it is derived not from the ingested protein, but from protein (or its split products) already in the body;

(2) Ammonia is one of the sources of urinary uric acid;

(3) The specific dynamic action of protein is composed of two factors, one constant, the other variable; the constant factor is the metabolism of the nitrogen; the variable factor is largely the metabolism of the deaminized residues.

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[2] Borsook, H., and Winegarden, H. M., *Proc. Nat. Acad. Sci.*, **17**, 75 (1931).
[3] Borsook, H., and Keighley, G. L., *Ibid.*, **19**, 626 (1933).
[4] Borsook, H., and Keighley, G. L., *Ibid.*, **19**, 720 (1933).
[5] Dock, W., personal communication.
[6] Rubner, M., *Die Gesetze des Energieverbrauchs bei der Ernährung*, Leipzig, 1902.
[7] Terroine, E. F., and Bonnet, R., *Bull. Soc. Chim. Biol.*, **8**, 976 (1926).
[8] Wilhelmj, C. M., and Mann, F. C., *Am. J. Physiol.*, **93**, 69 (1930).
[9] Wilhelmj, C. M., and Bollman, J. L., *J. Biol. Chem.*, **77**, 127 (1928).

ON THE MOTION OF GROWTH

VIII. The Connection between Growth and Heat Production in the Amphibian, *Bufo vulgaris*, from Fertilization to Metamorphosis

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Observations on growth that are limited solely to measurements of cumulative change in size are not of themselves sufficient to test the dynamical theory which applies, as we have previously shown, to human as well as to bacterial growth and metabolism.[1] Such an objective cannot, in fact, be achieved until records of size are supplemented by appropriate information in respect of energy exchange. Gayda's data[2] on the amphibian *Bufo vulgaris* also fulfil these conditions and they occupy, accordingly, a high place among similar observations on various other organisms thoroughly discussed by Needham.[3] In one respect Gayda's facts stand foremost; they possess the singular advantage of tracing the concomitant events of both growth and heat production from the moment